

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

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|--|---|---|------------------|
| Applicant's or agent's file reference F 8251/zi | FOR FURTHER ACTION | | See item 4 below |
| International application No. PCT/AT2005/000228 | International filing date (day/month/year) 24 June 2005 (24.06.2005) | Priority date (day/month/year) 25 June 2004 (25.06.2004) | |
| International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237 | | | |
| Applicant FIBREX MEDICAL RESEARCH & DEVELOPMENT GESMBH | | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).
2. This REPORT consists of a total of 5 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis.2).

Date of issuance of this report
28 December 2006 (28.12.2006)

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|---|---|
| The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70 | Authorized officer Yolaine Cussac e-mail: pt11@wipo.int |
|---|---|

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

TRANSLATION

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

| | | | |
|---|--|---|---|
| Applicant's or agent's file reference F 8251/zi | | Date of mailing (day/month/year) | See form PCT/ISA/210 |
| International application No. PCT/AT2005/000228 | | International filing date (day/month/year) 24.06.2005 | Priority date (day/month/year) 25.06.2004 |
| International Patent Classification (IPC) or both national classification and IPC A61K38/S6, A61P7/00, A61P9/00 | | | |
| Applicant FIBREX MEDICAL RESEARCH & DEVELOPMENT GESMBH | | | |

1. This opinion contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|--|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the opinion |
| <input type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input type="checkbox"/> | Box No. VIII | Certain observations on the international application |

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

| | |
|--|--------------------|
| Name and mailing address of the ISA/EP | Authorized officer |
| Facsimile No. | Telephone No. |

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AT2005/000228

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material
 a sequence listing
 table(s) related to the sequence listing
 - b. format of material
 in written format
 in computer readable form
 - c. time of filing/furnishing
 contained in the international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AT2005/000228

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|--------|--------|-----|
| Novelty (N) | Claims | 5-8 | YES |
| | Claims | 1-4, 9 | NO |
| Inventive step (IS) | Claims | 5-8 | YES |
| | Claims | 1-4, 9 | NO |
| Industrial applicability (IA) | Claims | 1-9 | YES |
| | Claims | - | NO |

2. Citations and explanations:

Reference is made to the following document:

D1 : WO 99/02565 A (THERASORB MEDIZINISCHE SYSTEME GMBH), 21 January 1999

1. Clarity of the claims, support by the description (PCT Article 5 and 6)

1.1 The phrase "which peptide possesses the biological property of matching the inducible VE-cadherin binding motif on the Bbeta chain (i.e. Bbeta 15-42) of human fibrin" in **claims 1, 7** is vague and unclear and leaves the reader uncertain as to the meaning of the technical feature in question. As a result, the subject matter of said claims is not clearly defined (PCT Article 6).

1.2 The amino acid sequence DKKREEAPSLRPA**PP**ISGGGYR in **claim 5** could possibly be lacking a proline radical and should possibly read DKKREEAPSLRPA**PPP**ISGGGYR.

1.3 In the present description the inhibiting effect of the peptides Bbeta15-42, Bbeta15-18, Bbeta15-26, Bbeta15-30, Bbeta15-34, Bbeta15-37 and Bbeta16-42 on the binding

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/AT2005/000228

Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

of the peptide Bbeta15-42 to VE-cadherin is indicated.

The activity of the peptide Bbeta15-42 in the treatment of mice infected with dengue virus and in the treatment of Gram-negative shock in rats is furthermore demonstrated.

However, therapeutic activity has not been demonstrated either for the shortened Bbeta peptides or further modified Bbeta peptides, or for the Aalpha peptide or for modified Aalpha peptides.

Consequently, the subject matter of **claims 1-4, 6, 7, 9** is considered to be insufficiently supported by the description and to be not disclosed clearly and completely over the entire scope of protection sought (PCT Article 5 and 6).

2. Novelty (PCT Article 33(2))

D1 discloses the use of the peptides GPR, GPRP, GPRV and GPRPERHES for the production of a medicament for treatment of diseases accompanied by microcirculation disorders, such as e.g. shock. Peptide GPRPERHES can be regarded as a peptide in which "Z5 is a peptide radical derived from the Aalpha or Bbeta chain of fibrin".

D1 therefore is prejudicial to the novelty of the subject matter of **claims 1-4, 9**.